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 NEWS  10 DEC 17   ELCOM reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  11 DEC 17   COMPUAB reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  12 DEC 17   SOLIDSTATE reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  13 DEC 17   CERAB reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
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L1 190 RP-8-BR-CAMPS

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L3 ANSWER 1 OF 12 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 97278969 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9133546
TITLE: Glucagon-like peptide I and glucose-dependent insulinotropic polypeptide stimulate Ca2+-induced secretion in rat alpha-cells by a protein kinase A-mediated mechanism.
AUTHOR: Ding W G; Renstrom E; Rorsman P; Buschard K; Gromada J
CORPORATE SOURCE: Department of Islet Cell Physiology, Kommunehospitalet, Copenhagen, Denmark.
SOURCE: Diabetes, **(1997 May)** 46 (5) 792-800.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970609
Last Updated on STN: 19970609
Entered Medline: 19970528

AB High-resolution capacitance measurements were used to explore the effects of the gut hormones GLP-I(7-36) amide [glucagon-like peptide I(7-36) amide] and GIP (glucose-dependent insulinotropic polypeptide) on Ca2+-dependent exocytosis in glucagon-secreting rat pancreatic alpha-cells. Both peptides produced a greater than threefold potentiation of secretion evoked by voltage-clamp depolarizations, an effect that was associated with an approximately 35% increase of the Ca2+ current. The stimulatory actions of GLP-I(7-36) amide and GIP were mimicked by forskolin and antagonized by the protein kinase A (PKA)-inhibitor **Rp-8-Br-cAMPS.** The islet hormone somatostatin inhibited the stimulatory action of GLP-I(7-36) amide and GIP

via a cyclic AMP-independent mechanism, whereas insulin had no effect on exocytosis. These data suggest that the alpha-cells are equipped with receptors for GLP-I and GIP and that these peptides, in addition to their well-established insulinotropic capacity, also stimulate glucagon secretion. We propose that the reported inhibitory action of GLP-I on glucagon secretion is accounted for by a paracrine mechanism (e.g., mediated by stimulated release of somatostatin that in turn suppresses exocytosis in the alpha-cell).

L3 ANSWER 2 OF 12 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 97271374 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9126325
TITLE: Extracellular ATP triggers cyclic AMP-dependent differentiation of HL-60 cells.
COMMENT: Republished in: Biochem Biophys Res Commun 1997 Jul 9;236(1):626-30
AUTHOR: Jiang L; Foster F M; Ward P; Tasevski V; Luttrell B M; Conigrave A D
CORPORATE SOURCE: Department of Biochemistry, University of Sydney, New South Wales, Australia.
SOURCE: Biochemical and biophysical research communications, **(1997 Mar 27)** 232 (3) 626-30.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970602
Last Updated on STN: 19980206
Entered Medline: 19970519
AB Extracellular ATP and ATP gamma S (1-1000 microM) stimulated cyclic AMP (cAMP) production in undifferentiated HL-60 cells. The potency order for adenine nucleotides and adenosine was ATP gamma S > ATP > > ADP > 3 AMP = Adenosine. Indomethacin (50 microM) had no effect on ATP-induced cAMP production. ATP and ATP gamma S also suppressed cell growth and induced differentiation as revealed by fMLP-stimulated beta-glucuronidase release 48 h after exposure. The potency order for the induction of fMLP-stimulated beta-glucuronidase release by adenine nucleotides and adenosine was ATP gamma S > 3 ATP > ADP > AMP = Adenosine approximately 0. The protein kinase A inhibitor **Rp-8-Br-cAMPS** (10-200 mM) suppressed ATP-induced differentiation but had no effect on ATP-dependent growth suppression. UTP which, like ATP, activates P2U receptors on HL-60 cells, had no effect on cAMP production, cell growth, or differentiation. The data suggest the existence of a novel receptor for ATP on undifferentiated HL-60 cells that is coupled to the activation of adenylate cyclase and cAMP-dependent differentiation.

L3 ANSWER 3 OF 12 MEDLINE on STN
ACCESSION NUMBER: 97366626 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9223456
TITLE: Extracellular ATP triggers cyclic AMP-dependent differentiation of HL-60 cells.
COMMENT: Republished from: Biochem Biophys Res Commun 1997 Mar 27;232(3): 626-30
AUTHOR: Jiang L; Foster F M; Ward P; Tasevski V; Luttrell B M; Conigrave A D
CORPORATE SOURCE: Department of Biochemistry, University of Sydney, New South Wales, Australia.
SOURCE: Biochemical and biophysical research communications, **(1997 Jul 9)** 236 (1) 626-30.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CORRECTED AND REPUBLISHED ARTICLE)
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970813
Last Updated on STN: 19970813
Entered Medline: 19970807

AB Extracellular ATP and ATPgammaS (1-1000 microM) stimulated cyclic AMP (cAMP) production in undifferentiated HL-60 cells. The potency order for adenine nucleotides and adenosine was ATPgammaS > ATP >> ADP > or = AMP = Adenosine. Indomethacin (50 microM) had no effect on ATP-induced cAMP production. ATP and ATPgammaS also suppressed cell growth and induced differentiation as revealed by fMLP-stimulated beta-glucuronidase release 48 h after exposure. The potency order for the induction of fMLP-stimulated beta-glucuronidase release by adenine nucleotides and adenosine was ATPgammaS > or = ATP > ADP > AMP = Adenosine approximately 0. The protein kinase A inhibitor **Rp-8-Br-cAMPS** (10-200 microM) suppressed ATP-induced differentiation but had no effect on ATP-dependent growth suppression. UTP which, like ATP, activates P2U receptors on HL-60 cells, had no effect on cAMP production, cell growth, or differentiation. The data suggest the existence of a novel receptor for ATP on undifferentiated HL-60 cells that is coupled to the activation of adenylate cyclase and cAMP-dependent differentiation.

L3 ANSWER 4 OF 12 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 97230223 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9075801
TITLE: Protein kinase A-dependent stimulation of exocytosis in mouse pancreatic beta-cells by glucose-dependent insulinotropic polypeptide.
AUTHOR: Ding W G; Gromada J
CORPORATE SOURCE: Department of Islet Cell Physiology, Novo Nordisk A/S, Copenhagen, Denmark.
SOURCE: Diabetes, **(1997 Apr)** 46 (4) 615-21.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 19970507
Entered Medline: 19970425

AB The mechanisms by which glucose-dependent insulinotropic polypeptide (GIP) stimulates insulin secretion were investigated by measurements of whole-cell Ca2+ currents, the cytoplasmic Ca2+ concentration, and cell capacitance as an indicator of exocytosis in individual mouse pancreatic beta-cells maintained in short-term culture. GIP produced a 4.2-fold potentiation of depolarization-induced exocytosis. This stimulation of exocytosis was not associated with a change in the whole-cell Ca2+-current, and there was only a small increase (30%) in the cytoplasmic Ca2+ concentration [intercellular free Ca2+([Ca2+]i)]. The stimulatory effect of GIP on exocytosis was blocked by pretreatment with the specific protein kinase A (PKA) inhibitor **Rp-8-Br-cAMPS.** Glucagon-like peptide-I(7-36) amide (GLP-I) stimulated exocytosis (90%) in the presence of a maximal GIP concentration (100 nmol/l). Replacement of GLP-I with forskolin produced a similar stimulatory action on exocytosis. These effects of GLP-I and forskolin in the presence of GIP did not involve a change in the whole-cell Ca2+-current or [Ca2+]i. GIP was ineffective in the presence of both forskolin and the phosphodiesterase inhibitor isobutylmethylxanthine (IBMX). Under the same experimental conditions, the protein kinase C (PKC)-activating phorbol ester 4-phorbol 12-myristate 13-acetate (PMA) stimulated exocytosis (60%). Collectively, our data indicate that the insulinotropic hormone GIP stimulates insulin secretion from pancreatic beta-cells, through the cAMP/PKA signaling pathway, by interacting with

the secretory machinery at a level distal to an elevation in [Ca2+]i.

L3 ANSWER 5 OF 12 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 97253408 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9098851
TITLE: Role of cyclic nucleotides in vasopressin-induced piglet pial artery dilation and opioid release.
AUTHOR: Rossberg M I; Armstead W M
CORPORATE SOURCE: Department of Anesthesia, University of Pennsylvania, Philadelphia, USA.
SOURCE: Pediatric research, **(1997 Apr)** 41 (4 Pt 1) 498-504.
Journal code: 0100714. ISSN: 0031-3998.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970716
Last Updated on STN: 19970716
Entered Medline: 19970702

AB It has previously been observed that the opioids methionine enkephalin and leucine enkephalin contribute to hypoxia-induced pial artery dilation in the piglet. It has also been demonstrated that vasopressin elicits pial artery dilation and contributes to hypoxia-induced pial dilation both directly and indirectly through the release of the above opioids. The present study was designed to investigate the role of cyclic nucleotides in this vasopressin-induced pial artery dilation and opioid release in newborn piglets equipped with a closed cranial window. Pial artery diameter and cortical periarachnoid cerebrospinal fluid (CSF) opioid and cyclic nucleotides were measured after topical application of vasopressin (40, 400, and 4000 pg/mL). Opioid levels and pial diameter were examined in the absence and presence of (Rp)-8-bromo-(Br)-cAMPs and (Rp)-8-Br-cGMPs, purported cAMP and cGMP antagonists, respectively. Periarachnoid cortical CSF cAMP concentration increased in response to topical vasopressin (1048 +/- 22, 1199 +/- 51, 1334 +/- 61 and 1453 +/- 59 fmol/mL for control, 40, 400, and 4000 pg/mL vasopressin, respectively, n = 9). Vasopressin elicited pial artery dilation, which was attenuated by **(Rp)-8-Br-cAMPs** (14 +/- 1, 22 +/- 1, and 29 +/- 2 versus 8 +/- 1, 12 +/- 2, and 18 +/- 2% dilation for 40, 400, 4000 pg/mL vasopressin, before and after **(Rp)-8-Br-cAMPs**, respectively, n = 7). Similarly, vasopressin-induced pial artery dilation was accompanied by elevated CSF cGMP and this dilation was attenuated in the presence of (Rp)-8-Br-cGMPs (13 +/- 1, 21 +/- 1, and 29 +/- 2 versus 5 +/- 1, 9 +/- 1, and 12 +/- 1% dilation for 40, 400, and 4000 pg/mL vasopressin before and after (Rp)-8-Br-cGMPs, respectively, n = 7). CSF opioid concentrations increased with topical vasopressin and these increases were attenuated by **(Rp)-8-Br-cAMPs.** CSF methionine enkephalin concentrations were 1193 +/- 60, 1530 +/- 63, 1937 +/- 89, and 2422 +/- 104 versus 1032 +/- 25, 1185 +/- 261, 1337 +/- 31, and 1519 +/- 44 pg/mL for control, 40, 400 and 4000 pg/mL vasopressin before and after **(Rp)-8-Br-cAMPs.** Similarly, vasopressin-induced CSF methionine enkephalin and leucine enkephalin release was attenuated in the presence of (Rp)-8-Br-cGMPs. These data show that both cAMP and cGMP contribute to vasopressin-induced pial artery dilation and the release of the opioids methionine enkephalin and leucine enkephalin.

L3 ANSWER 6 OF 12 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 97407805 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9264554
TITLE: Regulation of magnesium efflux from rat spleen lymphocytes.
AUTHOR: Wolf F I; Di Francesco A; Covacci V; Cittadini A
CORPORATE SOURCE: Institute of General Pathology and Giovanni XXIII Cancer

Research Centre, Universita Cattolica del Sacro Cuore, Rome, Italy.
SOURCE: Archives of biochemistry and biophysics, **(1997 Aug 15)** 344 (2) 397-403.
Journal code: 0372430. ISSN: 0003-9861.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970922
Last Updated on STN: 19980206
Entered Medline: 19970908

AB Rat spleen lymphocytes (RSL) incubated at 37 degrees C in Mg-free medium (0-trans conditions) exibited Mg2+ efflux with apparent velocity of 0.2 nmol/mg protein/min. After 30 min, this process accounted for the mobilization of about 15% of cell total Mg2+. Half of the Mg2+ efflux depended on extracellular Na+ and was stimulated by cAMP. IFN-alpha significantly enhanced Mg2+ efflux under 0-trans conditions as well as in the presence of physiological extracellular Mg2+. Pretreatment of RSL with indomethacin completely abolished IFN-alpha-induced Mg2+ efflux, suggesting a crucial role for cyclooxygenase-dependent arachidonate metabolism. On the other hand, pretreatment of RSL with the PKA inhibitor **(Rp)8-Br-cAMPS** prevented IFN-alpha stimulation of Mg2+ efflux, indicating the involvement of cAMP. Consistently, both IFN-alpha and exogenous PGE1 increased cAMP from 50 to 125 pmol/mg protein. Altogether these results show that IFN-alpha stimulates Mg2+ efflux by activating arachidonate metabolism and synthesis of prostaglandins. By influencing adenylcyclase activity, PGEs can eventually promote cAMP-dependent Mg2+ efflux, possibly through the activity of a Na-Mg antiport. In RSL, therefore, magnesium movements can be under the control of IFN-alpha and, perhaps, of other cytokines, suggesting the involvement of Mg2+ in cell response to receptor-mediated stimuli.

L3 ANSWER 7 OF 12 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 97236273 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9125131
TITLE: Fas/APO-1(CD95)-induced apoptosis of primary hepatocytes is inhibited by cAMP.
AUTHOR: Fladmark K E; Gjertsen B T; Doskeland S O; Vintermyr O K
CORPORATE SOURCE: Department of Anatomy and Cell Biology, University of Bergen, Norway.
SOURCE: Biochemical and biophysical research communications, **(1997 Mar 6)** 232 (1) 20-5.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970506
Last Updated on STN: 19970506
Entered Medline: 19970422

AB Fas/APO-1(CD-95) activation induced rapid apoptotic cell death of primary rat hepatocytes in suspension culture. Activators of cAMP-dependent protein kinase (glucagon and N6-benzoyl-cAMP) protected against apoptosis, whereas the specific cAMP-kinase inhibitor **(Rp)-8-Br-cAMPS** enhanced Fas-induced death. The latter observation indicated that even the basal cAMP level may provide partial protection against Fas-induced hepatocyte apoptosis. Two-dimensional gel electrophoresis revealed decreased phosphorylation of several proteins in Fas-activated cells. Most of these dephosphorylations were attenuated or not observed in cells simultaneously stimulated by anti-Fas and cAMP, indicating a tight correlation between the dephosphorylations and death.

Elevation of cAMP rescued the cells not only from the Fas-induced morphological changes and dephosphorylation, but also from functional deterioration. Whereas cells treated with anti-Fas alone quickly lost plating efficiency, hepatocytes co-treated with glucagon retained their ability to adhere and spread on a collagen substratum.

L3 ANSWER 8 OF 12 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 95386509 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7657638
TITLE: Novel (Rp)-cAMPS analogs as tools for inhibition of cAMP-kinase in cell culture. Basal cAMP-kinase activity modulates interleukin-1 beta action.
AUTHOR: Gjertsen B T; Mellgren G; Otten A; Maronde E; Genieser H G; Jastorff B; Vintermyr O K; McKnight G S; Doskeland S O
CORPORATE SOURCE: Department of Anatomy and Cell Biology, University of Bergen, Norway.
CONTRACT NUMBER: GM 32875 (NIGMS)
ML 44948
SOURCE: Journal of biological chemistry, **(1995 Sep 1)** 270 (35) 20599-607.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951013
Last Updated on STN: 19970203
Entered Medline: 19951004

AB Novel (Rp)-cAMPS analogs differed widely in ability to antagonize cAMP activation of pure cAMP-dependent protein kinase I and II and to antagonize actions of cAMP on gene expression, shape change, apoptosis, DNA replication, and protein phosphorylation in intact cells. These differences were related to different abilities of the analogs to stabilize the holoenzyme form relative to the dissociated form of cAMP kinase type I and II. **(Rp)-8-Br-cAMPS** and (Rp)-8-Cl-cAMPS were the most potent cAMP antagonists for isolated type I kinase and for cells expressing mostly type I kinase, like IPC-81 leukemia cells, fibroblasts transfected with type I regulatory subunit (RI), and primary hepatocytes. It is proposed that **(Rp)-8-Br-cAMPS** or (Rp)-8-Cl-cAMPS should replace (Rp)-cAMPS as the first line cAMP antagonist, particularly for studies in cells expressing predominantly type I kinase. The phosphorylation of endogenous hepatocyte proteins was affected oppositely by **(Rp)-8-Br-cAMPS** and increased cAMP, indicating that **(Rp)-8-Br-cAMPS** inhibited basal cAMP-kinase activity. The inhibition of basal kinase activity was accompanied by enhanced DNA replication, an effect which could be reproduced by microinjected mutant cAMP-subresponsive RI. It is concluded that the basal cAMP-kinase activity exerts a tonic inhibition of hepatocyte replication. **(Rp)-8-Br-cAMPS** and microinjected RI also desensitized hepatocytes toward inhibition of DNA synthesis by interleukin-1 beta. This indicates that basal cAMP-kinase activity can have a permissive role for the action of another (interleukin-1 beta) signaling pathway.

L3 ANSWER 9 OF 12 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 95301553 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7782324
TITLE: Regulation of RCK1 currents with a cAMP analog via enhanced protein synthesis and direct channel phosphorylation.
AUTHOR: Levin G; Keren T; Peretz T; Chikvashvili D; Thornhill W B; Lotan I
CORPORATE SOURCE: Department of Physiology and Pharmacology, Sackler School

of Medicine, Tel-Aviv University, Ramat Aviv, Israel.
CONTRACT NUMBER: NS-29633 (NINDS)
SOURCE: Journal of biological chemistry, **(1995 Jun 16)** 270 (24) 14611-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199507
ENTRY DATE: Entered STN: 19950726
Last Updated on STN: 19950726
Entered Medline: 19950717

AB We have recently shown that the rat brain Kv1.1 (RCK1) voltage-gated K+ channel is partially phosphorylated in its basal state in Xenopus oocytes and can be further phosphorylated upon treatment for a short time with a cAMP analog (Ivanina, T., Perts, T., Thornhill, W. B., Levin, G., Dascal, N., and Lotan, I. (1994) Biochemistry 33, 8786-8792). In this study, we show, by two-electrode voltage clamp analysis, that whereas treatments for a short time with various cAMP analogs do not affect the channel function, prolonged treatment with 8-bromoadenosine 3',5'-cyclic monophosphorothioate ((Sp)-8-Br-cAMPS), a membrane-permeant cAMP analog, enhances the current amplitude. It also enhances the current amplitude through a mutant channel that cannot be phosphorylated by protein kinase A activation. The enhancement is inhibited in the presence of (**Rp**)-**8-Br-cAMPS**, a membrane-permeant protein kinase A inhibitor. Concomitant SDS-polyacrylamide gel electrophoresis analysis reveals that this treatment not only brings about phosphorylation of the wild-type channel, but also increases the amounts of both wild-type and mutant channel proteins; the latter effect can be inhibited by cycloheximide, a protein synthesis inhibitor. In the presence of cycloheximide, the (Sp)-8-Br-cAMPS treatment enhances only the wild-type current amplitudes and induces accumulation of wild-type channels in the plasma membrane of the oocyte. In summary, prolonged treatment with (Sp)-8-Br-cAMPS regulates RCK1 function via two pathways, a pathway leading to enhanced channel synthesis and a pathway involving channel phosphorylation that directs channels to the plasma membrane.

L3 ANSWER 10 OF 12 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 95165158 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7861174
TITLE: Effects of arachidonic acid on dopamine synthesis, spontaneous release, and uptake in striatal synaptosomes from the rat.
AUTHOR: L'hirondel M; Cheramy A; Godeheu G; Glowinski J
CORPORATE SOURCE: INSERM U114, College de France, Paris.
SOURCE: Journal of neurochemistry, **(1995 Mar)** 64 (3) 1406-9.
Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950404
Last Updated on STN: 19950404
Entered Medline: 19950317

AB Arachidonic acid (AA) markedly stimulated, in a dose-dependent manner, the spontaneous release of [3H]dopamine ([3H]DA) continuously synthesized from [3H]tyrosine in purified synaptosomes from the rat striatum. As estimated by simultaneous measurement of the rate of [3H]H2O formation (an index of [3H]tyrosine conversion into [3H]DOPA), the AA response was associated with a progressive and dose-dependent reduction of [3H]DA synthesis. In contrast to AA, arachidonic acid, oleic acid, and the methyl ester of AA (all at 10(-4) M) did not modify [3H]DA release. The AA (3 x 10(-5)

M)-evoked release of [3H]DA was not affected by inhibiting AA metabolism, with either 5,8,11,14-eicosatetraynoic acid or metyrapone, suggesting that AA acts directly and not through one of its metabolites. AA also inhibited in a dose-dependent manner [3H]DA uptake into synaptosomes, with a complete blockade observed at 10(-4) M. However, AA (10(-4) M) still stimulated [3H]DA spontaneous release in the presence of either nomifensine or other DA uptake inhibitors, indicating that AA both inhibits DA reuptake and facilitates its release process. Finally, the AA (10(-4) M)-evoked release of [3H]DA was not affected by protein kinase A inhibitors (H-89 or **Rp-8-Br-cAMPS**)
but was markedly reduced in the presence of protein kinase C inhibitors (Ro 31-7549 or chelerythrine).

L3 ANSWER 11 OF 12 MEDLINE on STN
ACCESSION NUMBER: 96012478 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7572340
TITLE: Hormonal control of hepatic glutaminase.
AUTHOR: Brosnan J T; Ewart H S; Squires S A
CORPORATE SOURCE: Department of Biochemistry, Memorial University of Newfoundland, St. John's, Canada.
SOURCE: Advances in enzyme regulation, **(1995)** 35 131-46.
Journal code: 0044263. ISSN: 0065-2571.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19980206
Entered Medline: 19951026

AB (1) Glucagon activates hepatic glutaminase in vivo. Mitochondria from glucagon-injected rats retain an enhanced capacity to catabolize glutamine and this is more sensitive to activation by inorganic phosphate. The glucagon-elicited stimulation of glutaminase is not evident in broken mitochondria. A similar activation of glutaminase occurs in a number of situations which are associated with elevated glucagon levels in vivo, i.e., after a high-protein meal, after injection of bacterial endotoxin and in diabetes mellitus. (2) Studies in isolated hepatocytes revealed that glutaminase could be activated, not only by glucagon, but also by a cell-permeable protein kinase A activator (Sp-cAMPS) and by a cell-permeable protein phosphatase 1 and 2A inhibitor (okadaic acid). However, the activation of glutaminase by glucagon was not inhibited by a cell-permeable protein kinase A inhibitor (**Rp-8-Br-cAMPS**). We suggest that the signalling pathway, for glutaminase activation by glucagon, is complex and possibly contains redundant elements.

L3 ANSWER 12 OF 12 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 94235325 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8179921
TITLE: Theophylline suppresses human alveolar macrophage respiratory burst through phosphodiesterase inhibition.
AUTHOR: Dent G; Giembycz M A; Rabe K F; Wolf B; Barnes P J; Magnussen H
CORPORATE SOURCE: Krankenhaus Grosshansdorf, LVA Hamburg, Germany.
SOURCE: American journal of respiratory cell and molecular biology, **(1994 May)** 10 (5) 565-72.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940621
Last Updated on STN: 19940621

Entered Medline: 19940614

AB The effects of theophylline upon human alveolar macrophage function were assessed and compared with its action upon macrophage cyclic nucleotide phosphodiesterase (PDE) activity and cyclic adenosine monophosphate (cAMP) levels. In the concentration range of 10 mumol/liter to 1 mmol/liter, theophylline caused a concentration-dependent inhibition of opsonized zymosan-stimulated hydrogen peroxide (H2O2) generation and PDE-catalyzed cAMP hydrolysis and increased the cellular cAMP content. Macrophage H2O2 generation was also inhibited by forskolin, an activator of adenylyl cyclase, but whereas theophylline (1 mmol/liter) and forskolin (1 mumol/liter) exhibited a synergic elevation of macrophage cAMP, there was no synergy between the two agents in the inhibition of respiratory burst. The inhibition of H2O2 generation by theophylline was reversed by the competitive inhibitor of cAMP-dependent protein kinase, (Rp)8-bromoadenosine cyclic 3':5'-monophosphorothioate (**Rp-8-Br-cAMPS**; 100 mumol/liter), indicating that the functional effect of theophylline was mediated through the elevation of cAMP. The inhibition of H2O2 generation by theophylline was not affected by adenosine deaminase (0.1 U/ml), indicating that the inhibition did not involve adenosine antagonism. It is concluded that theophylline exerts a direct inhibitory action upon human alveolar macrophage function through the elevation of cAMP levels as a result of PDE inhibition, and that this effect is observed at concentrations of theophylline that may be achieved in serum during therapy.

=> s (rp()8()br()monobutyryl()camps) or (rp()monobutyryl()camps) or (rp()8()4()chlorophenyl()thio()camps) or (rp()piperidino(
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nested terms that are not separated by a logical operator.

=> s (rp()8()br()monobutyryl()camps) or (rp()monobutyryl()camps) or (rp()8()4()chlorophenyl()thio()camps) or (rp()piperidino()camps)
L4 0 (RP(W) 8(W) BR(W) MONOBUTYRYL(W) CAMPS) OR (RP(W) MONOBUTYRYL(W) CAMPS) OR (RP(W) 8(W) 4(W) CHLOROPHENYL(W) THIO(W) CAMPS) OR (RP(W) PIPERIDINO(W) CAMPS)

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FULL ESTIMATED COST	62.52	63.99

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    62.52      63.99

=> S RP-8-BR-MONOBUTYRYL-CAMPS
L5            0 RP-8-BR-MONOBUTYRYL-CAMPS

=> S MONOBUTYRYL-CAMPS
L6            0 MONOBUTYRYL-CAMPS

=> S rp(5n)CAMPS
L7         2677 RP(5N) CAMPS

=> S rp-8(5n)CAMPS
L8          397 RP-8(5N) CAMPS

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9           116 DUP REM L8 (281 DUPLICATES REMOVED)

=> s l9 and py<1998
   2 FILES SEARCHED...
   4 FILES SEARCHED...
L10          25 L9 AND PY<1998

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L10  ANSWER 1 OF 25     MEDLINE on STN
ACCESSION NUMBER:    97407805     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 9264554
TITLE:               Regulation of magnesium efflux from rat spleen lymphocytes.
AUTHOR:              Wolf F I; Di Francesco A; Covacci V; Cittadini A
CORPORATE SOURCE:    Institute of General Pathology and Giovanni XXIII Cancer
                     Research Centre, Universita Cattolica del Sacro Cuore,
                     Rome, Italy.
SOURCE:              Archives of biochemistry and biophysics, (1997 Aug
                     15) 344 (2) 397-403.
                     Journal code: 0372430. ISSN: 0003-9861.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199709
ENTRY DATE:          Entered STN: 19970922
                     Last Updated on STN: 19980206
                     Entered Medline: 19970908
AB   Rat spleen lymphocytes (RSL) incubated at 37 degrees C in Mg-free medium
     (O-trans conditions) exibited Mg2+ efflux with apparent velocity of 0.2
     nmol/mg protein/min.  After 30 min, this process accounted for the
     mobilization of about 15% of cell total Mg2+.  Half of the Mg2+ efflux
     depended on extracellular Na+ and was stimulated by cAMP.  IFN-alpha
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significantly enhanced Mg2+ efflux under O-trans conditions as well as in the presence of physiological extracellular Mg2+. Pretreatment of RSL with indomethacin completely abolished IFN-alpha-induced Mg2+ efflux, suggesting a crucial role for cyclooxygenase-dependent arachidonate metabolism. On the other hand, pretreatment of RSL with the PKA inhibitor (**Rp**)**8**-Br-**cAMPS** prevented IFN-alpha stimulation of Mg2+ efflux, indicating the involvement of cAMP. Consistently, both IFN-alpha and exogenous PGE1 increased cAMP from 50 to 125 pmol/mg protein. Altogether these results show that IFN-alpha stimulates Mg2+ efflux by activating arachidonate metabolism and synthesis of prostaglandins. By influencing adenylcyclase activity, PGEs can eventually promote cAMP-dependent Mg2+ efflux, possibly through the activity of a Na-Mg antiport. In RSL, therefore, magnesium movements can be under the control of IFN-alpha and, perhaps, of other cytokines, suggesting the involvement of Mg2+ in cell response to receptor-mediated stimuli.

L10 ANSWER 2 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97393082 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9249599
TITLE: Osmo-mechanically sensitive phosphatidylinositol signaling regulates a Ca2+ influx channel in renal epithelial cells.
AUTHOR: O'Neil R G; Leng L
CORPORATE SOURCE: Department of Integrative Biology, University of Texas-Houston Health Science Center 77030, USA.
CONTRACT NUMBER: DK-40545 (NIDDK)
SOURCE: American journal of physiology, **(1997 Jul)** 273 (1 Pt 2) F120-8.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970916
Last Updated on STN: 20000303
Entered Medline: 19970903

AB Regulation of dihydropyridine (nifedipine)-sensitive calcium influx was studied in rabbit culture proximal tubule cells using the fura 2 fluorescence ratio technique. "Osmo-mechanically induced" swelling of cells by exposure to hypotonic medium (220 mosmol/kgH2O) caused a rapid rise in intracellular calcium that was predominantly due to influx of calcium via both dihydropyridine-sensitive (nifedipine-sensitive) and -insensitive calcium influx pathways. The dihydropyridine-sensitive pathway was regulated, in part, by the phosphatidylinositol signaling pathway. Inhibition of phospholipase C by treatment with 2-nitro-4-carboxyphenyl-N,N-diphenylcarbamate (NCDC), inhibition of protein kinase C (PKC) by staurosporine, or long-term (24 h) treatment with phorbol 12-myristate 13-acetate (PMA) to downregulate PKC abolished most of the osmo-induced, dihydropyridine-sensitive calcium influx signal. Short-term (seconds) PMA treatment to activate PKC produced a marked stimulation of both dihydropyridine-sensitive and -insensitive calcium influx in isotonic (2- to 3-fold stimulation) and hypotonic (5-fold stimulation) conditions. In contrast, elevation of adenosine 3',5'-cyclic monophosphate (cAMP) by treatment with forskolin or inhibition of protein kinase A (PKA) by treatment with the cAMP analog, **Rp**-**8**-CPT-**cAMPS** (the Rp diastereoisomer of adenosine 3',5'-cyclic monophosphothionate), had little or no influence on calcium influx, including dihydropyridine-sensitive calcium influx. It is concluded that osmo-mechanical stress activates a dihyropyridine-sensitive calcium influx pathway that is predominantly regulated via the phosphatidylinositol signaling pathway and PKC and not through the cAMP/PKA signaling pathway.

L10 ANSWER 3 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97366626 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9223456
TITLE: Extracellular ATP triggers cyclic AMP-dependent differentiation of HL-60 cells.
COMMENT: Republished from: Biochem Biophys Res Commun 1997 Mar 27;232(3): 626-30
AUTHOR: Jiang L; Foster F M; Ward P; Tasevski V; Luttrell B M; Conigrave A D
CORPORATE SOURCE: Department of Biochemistry, University of Sydney, New South Wales, Australia.
SOURCE: Biochemical and biophysical research communications, **(1997 Jul 9)** 236 (1) 626-30.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CORRECTED AND REPUBLISHED ARTICLE)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970813
Last Updated on STN: 19970813
Entered Medline: 19970807

AB Extracellular ATP and ATPgammaS (1-1000 microM) stimulated cyclic AMP (cAMP) production in undifferentiated HL-60 cells. The potency order for adenine nucleotides and adenosine was ATPgammaS > ATP >> ADP > or = AMP = Adenosine. Indomethacin (50 microM) had no effect on ATP-induced cAMP production. ATP and ATPgammaS also suppressed cell growth and induced differentiation as revealed by fMLP-stimulated beta-glucuronidase release 48 h after exposure. The potency order for the induction of fMLP-stimulated beta-glucuronidase release by adenine nucleotides and adenosine was ATPgammaS > or = ATP > ADP > AMP = Adenosine approximately 0. The protein kinase A inhibitor **Rp-8**-Br-**cAMPS** (10-200 microM) suppressed ATP-induced differentiation but had no effect on ATP-dependent growth suppression. UTP which, like ATP, activates P2U receptors on HL-60 cells, had no effect on cAMP production, cell growth, or differentiation. The data suggest the existence of a novel receptor for ATP on undifferentiated HL-60 cells that is coupled to the activation of adenylate cyclase and cAMP-dependent differentiation.

L10 ANSWER 4 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97278969 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9133546
TITLE: Glucagon-like peptide I and glucose-dependent insulinotropic polypeptide stimulate Ca2+-induced secretion in rat alpha-cells by a protein kinase A-mediated mechanism.
AUTHOR: Ding W G; Renstrom E; Rorsman P; Buschard K; Gromada J
CORPORATE SOURCE: Department of Islet Cell Physiology, Kommunehospitalet, Copenhagen, Denmark.
SOURCE: Diabetes, **(1997 May)** 46 (5) 792-800.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970609
Last Updated on STN: 19970609
Entered Medline: 19970528

AB High-resolution capacitance measurements were used to explore the effects of the gut hormones GLP-I(7-36) amide [glucagon-like peptide I(7-36) amide] and GIP (glucose-dependent insulinotropic polypeptide) on Ca2+-dependent exocytosis in glucagon-secreting rat pancreatic alpha-cells. Both peptides produced a greater than threefold potentiation of secretion evoked by voltage-clamp depolarizations, an effect that was associated with an approximately 35% increase of the Ca2+ current. The

stimulatory actions of GLP-I(7-36) amide and GIP were mimicked by forskolin and antagonized by the protein kinase A (PKA)-inhibitor **Rp-8-Br-cAMPS.** The islet hormone somatostatin inhibited the stimulatory action of GLP-I(7-36) amide and GIP via a cyclic AMP-independent mechanism, whereas insulin had no effect on exocytosis. These data suggest that the alpha-cells are equipped with receptors for GLP-I and GIP and that these peptides, in addition to their well-established insulinotropic capacity, also stimulate glucagon secretion. We propose that the reported inhibitory action of GLP-I on glucagon secretion is accounted for by a paracrine mechanism (e.g., mediated by stimulated release of somatostatin that in turn suppresses exocytosis in the alpha-cell).

L10 ANSWER 5 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97271374 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9126325
TITLE: Extracellular ATP triggers cyclic AMP-dependent differentiation of HL-60 cells.
COMMENT: Republished in: Biochem Biophys Res Commun 1997 Jul 9;236(1):626-30
AUTHOR: Jiang L; Foster F M; Ward P; Tasevski V; Luttrell B M; Conigrave A D
CORPORATE SOURCE: Department of Biochemistry, University of Sydney, New South Wales, Australia.
SOURCE: Biochemical and biophysical research communications, **(1997 Mar 27)** 232 (3) 626-30.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970602
Last Updated on STN: 19980206
Entered Medline: 19970519

AB Extracellular ATP and ATP gamma S (1-1000 microM) stimulated cyclic AMP (cAMP) production in undifferentiated HL-60 cells. The potency order for adenine nucleotides and adenosine was ATP gamma S > ATP > > ADP > 3 AMP = Adenosine. Indomethacin (50 microM) had no effect on ATP-induced cAMP production. ATP and ATP gamma S also suppressed cell growth and induced differentiation as revealed by fMLP-stimulated beta-glucuronidase release 48 h after exposure. The potency order for the induction of fMLP-stimulated beta-glucuronidase release by adenine nucleotides and adenosine was ATP gamma S > 3 ATP > ADP > AMP = Adenosine approximately 0. The protein kinase A inhibitor **Rp-8-Br-cAMPS** (10-200 mM) suppressed ATP-induced differentiation but had no effect on ATP-dependent growth suppression. UTP which, like ATP, activates P2U receptors on HL-60 cells, had no effect on cAMP production, cell growth, or differentiation. The data suggest the existence of a novel receptor for ATP on undifferentiated HL-60 cells that is coupled to the activation of adenylate cyclase and cAMP-dependent differentiation.

L10 ANSWER 6 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97253408 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9098851
TITLE: Role of cyclic nucleotides in vasopressin-induced piglet pial artery dilation and opioid release.
AUTHOR: Rossberg M I; Armstead W M
CORPORATE SOURCE: Department of Anesthesia, University of Pennsylvania, Philadelphia, USA.
SOURCE: Pediatric research, **(1997 Apr)** 41 (4 Pt 1) 498-504.
Journal code: 0100714. ISSN: 0031-3998.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970716
Last Updated on STN: 19970716
Entered Medline: 19970702

AB It has previously been observed that the opioids methionine enkephalin and leucine enkephalin contribute to hypoxia-induced pial artery dilation in the piglet. It has also been demonstrated that vasopressin elicits pial artery dilation and contributes to hypoxia-induced pial dilation both directly and indirectly through the release of the above opioids. The present study was designed to investigate the role of cyclic nucleotides in this vasopressin-induced pial artery dilation and opioid release in newborn piglets equipped with a closed cranial window. Pial artery diameter and cortical periarachnoid cerebrospinal fluid (CSF) opioid and cyclic nucleotides were measured after topical application of vasopressin (40, 400, and 4000 pg/mL). Opioid levels and pial diameter were examined in the absence and presence of **(Rp)-8**-bromo-(Br)-**cAMPs** and **(Rp)-8**-Br-cGMPs, purported cAMP and cGMP antagonists, respectively. Periarachnoid cortical CSF cAMP concentration increased in response to topical vasopressin (1048 +/- 22, 1199 +/- 51, 1334 +/- 61 and 1453 +/- 59 fmol/mL for control, 40, 400, and 4000 pg/mL vasopressin, respectively, n = 9). Vasopressin elicited pial artery dilation, which was attenuated by **(Rp)-8**-Br-**cAMPs** (14 +/- 1, 22 +/- 1, and 29 +/- 2 versus 8 +/- 1, 12 +/- 2, and 18 +/- 2% dilation for 40, 400, 4000 pg/mL vasopressin, before and after **(Rp)-8**-Br-**cAMPs**, respectively, n = 7). Similarly, vasopressin-induced pial artery dilation was accompanied by elevated CSF cGMP and this dilation was attenuated in the presence of (Rp)-8-Br-cGMPs (13 +/- 1, 21 +/- 1, and 29 +/- 2 versus 5 +/- 1, 9 +/- 1, and 12 +/- 1% dilation for 40, 400, and 4000 pg/mL vasopressin before and after (Rp)-8-Br-cGMPs, respectively, n = 7). CSF opioid concentrations increased with topical vasopressin and these increases were attenuated by **(Rp)-8**-Br-**cAMPs.** CSF methionine enkephalin concentrations were 1193 +/- 60, 1530 +/- 63, 1937 +/- 89, and 2422 +/- 104 versus 1032 +/- 25, 1185 +/- 261, 1337 +/- 31, and 1519 +/- 44 pg/mL for control, 40, 400 and 4000 pg/mL vasopressin before and after **(Rp)-8**-Br-**cAMPs.** Similarly, vasopressin-induced CSF methionine enkephalin and leucine enkephalin release was attenuated in the presence of (Rp)-8-Br-cGMPs. These data show that both cAMP and cGMP contribute to vasopressin-induced pial artery dilation and the release of the opioids methionine enkephalin and leucine enkephalin.

L10 ANSWER 7 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97242588 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9087587
TITLE: Iloprost dilates rat small arteries: role of K(ATP)- and K(Ca)-channel activation by cAMP-dependent protein kinase.
AUTHOR: Schubert R; Serebryakov V N; Mewes H; Hopp H H
CORPORATE SOURCE: Faculty of Medicine, University of Rostock, Germany.
SOURCE: American journal of physiology, **(1997 Mar)** 272 (3 Pt 2) H1147-56.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 19980206
Entered Medline: 19970428

AB The effect of the stable prostacyclin analog iloprost and its mechanism of action were investigated with the use of pressurized rat tail small arteries with a spontaneous myogenic tone. Iloprost concentration

dependently dilated these vessels with a half-maximal effective dose of 5.0 +/- 0.5 x 10(-8) M. Application of 10(-7)-10(-6) M glibenclamide, a blocker of ATP-sensitive potassium (K(ATP)) channels, inhibited the iloprost-induced dilation. Glibenclamide did not affect the basal vessel diameter. The application of 5 x 10(-5)-10(-3) M tetraethylammonium (TEA) and 5 x 10(-9)-10(-7) M iberiotoxin, blockers of calcium-activated potassium (K(Ca)) channels, decreased vessel diameter in the presence of iloprost. Both TEA and iberiotoxin reduced the basal vessel diameter. Glibenclamide at 10(-6) M inhibited the dilation produced by 5 x 10(-5) M Sp-5,6-DCl-cBIMPS, an activator of adenosine 3',5'-cyclic monophosphate (cAMP)-dependent protein kinase. Iberiotoxin at 10(-7) M decreased vessel diameter in the presence of Sp-5,6-DCl-cBIMPS. H-89 and **Rp-8-CPT-cAMPS**, blockers of cAMP-dependent protein kinase A (PKA), inhibited the iloprost-induced dilation of these vessels. With use of the whole cell configuration of the patch-clamp technique, it was observed that 5 x 10(-7) M iloprost enhanced an outward current, determined largely by K(Ca) channels, 1.79 +/- 0.17-fold in freshly isolated smooth muscle cells from rat tail small artery. These data show that iloprost dilates rat tail small arteries with a spontaneous myogenic tone and suggest that K(ATP) as well as K(Ca) channels are involved in this effect, which is mediated, at least partly, by PKA.

L10 ANSWER 8 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97236273 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9125131
TITLE: Fas/APO-1(CD95)-induced apoptosis of primary hepatocytes is inhibited by cAMP.
AUTHOR: Fladmark K E; Gjertsen B T; Doskeland S O; Vintermyr O K
CORPORATE SOURCE: Department of Anatomy and Cell Biology, University of Bergen, Norway.
SOURCE: Biochemical and biophysical research communications, **(1997 Mar 6)** 232 (1) 20-5.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970506
Last Updated on STN: 19970506
Entered Medline: 19970422

AB Fas/APO-1(CD-95) activation induced rapid apoptotic cell death of primary rat hepatocytes in suspension culture. Activators of cAMP-dependent protein kinase (glucagon and N6-benzoyl-cAMP) protected against apoptosis, whereas the specific cAMP-kinase inhibitor **(Rp)-8-Br-cAMPS** enhanced Fas-induced death. The latter observation indicated that even the basal cAMP level may provide partial protection against Fas-induced hepatocyte apoptosis. Two-dimensional gel electrophoresis revealed decreased phosphorylation of several proteins in Fas-activated cells. Most of these dephosphorylations were attenuated or not observed in cells simultaneously stimulated by anti-Fas and cAMP, indicating a tight correlation between the dephosphorylations and death. Elevation of cAMP rescued the cells not only from the Fas-induced morphological changes and dephosphorylation, but also from functional deterioration. Whereas cells treated with anti-Fas alone quickly lost plating efficiency, hepatocytes co-treated with glucagon retained their ability to adhere and spread on a collagen substratum.

L10 ANSWER 9 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97230223 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9075801
TITLE: Protein kinase A-dependent stimulation of exocytosis in mouse pancreatic beta-cells by glucose-dependent insulinotropic polypeptide.
AUTHOR: Ding W G; Gromada J

CORPORATE SOURCE: Department of Islet Cell Physiology, Novo Nordisk A/S, Copenhagen, Denmark.
SOURCE: Diabetes, **(1997 Apr)** 46 (4) 615-21.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 19970507
Entered Medline: 19970425

AB The mechanisms by which glucose-dependent insulinotropic polypeptide (GIP) stimulates insulin secretion were investigated by measurements of whole-cell Ca2+ currents, the cytoplasmic Ca2+ concentration, and cell capacitance as an indicator of exocytosis in individual mouse pancreatic beta-cells maintained in short-term culture. GIP produced a 4.2-fold potentiation of depolarization-induced exocytosis. This stimulation of exocytosis was not associated with a change in the whole-cell Ca2+-current, and there was only a small increase (30%) in the cytoplasmic Ca2+ concentration [intercellular free Ca2+([Ca2+]i)]. The stimulatory effect of GIP on exocytosis was blocked by pretreatment with the specific protein kinase A (PKA) inhibitor **Rp-8-Br-cAMPS**
. Glucagon-like peptide-I(7-36) amide (GLP-I) stimulated exocytosis (90%) in the presence of a maximal GIP concentration (100 nmol/l). Replacement of GLP-I with forskolin produced a similar stimulatory action on exocytosis. These effects of GLP-I and forskolin in the presence of GIP did not involve a change in the whole-cell Ca2+-current or [Ca2+]i. GIP was ineffective in the presence of both forskolin and the phosphodiesterase inhibitor isobutylmethylxanthine (IBMX). Under the same experimental conditions, the protein kinase C (PKC)-activating phorbol ester 4-phorbol 12-myristate 13-acetate (PMA) stimulated exocytosis (60%). Collectively, our data indicate that the insulinotropic hormone GIP stimulates insulin secretion from pancreatic beta-cells, through the cAMP/PKA signaling pathway, by interacting with the secretory machinery at a level distal to an elevation in [Ca2+]i.

L10 ANSWER 10 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97197704 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9046000
TITLE: Role of activation of calcium-sensitive K+ channels and cAMP in opioid-induced pial artery dilation.
AUTHOR: Armstead W M
CORPORATE SOURCE: Department of Anesthesia and Pharmacology, The University of Pennsylvania , USA.
SOURCE: Brain research, **(1997 Feb 7)** 747 (2) 252-8.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970609
Last Updated on STN: 19970609
Entered Medline: 19970527

AB The present study was designed to investigate the role of activation of Kca+2 channels and cAMP in opioid-induced pial artery dilation in newborn pigs equipped with closed cranial windows. Methionine enkephalin, an endogenous mu agonist, elicited dilation that was modestly attenuated by the Kca+2 channel antagonist, iberiotoxin (10(-7) M) (7 +/- 1, 11 +/- 1 and 16 +/- 1 vs. 4 +/- 1, 7 +/- 1, and 11 +/- 1% for methionine enkephalin 10(-10), 10(-8), 10(-6) M in the absence and presence of iberiotoxin, respectively). Dilator responses to leucine enkephalin and dynorphin, endogenous delta and kappa agonists, as well as the synthetic analogues DAMGO, DPDPE, deltorphin and U50488H all were similarly attenuated by

iberiotoxin. Dilation in response to methionine enkephalin was accompanied by increased CSF cAMP concentration (1170 +/- 21, 1358 +/- 22, 1473 +/- 26, and 1575 +/- 24 fmol/ml for control, 10(-10), 10(-8), 10(-6) M methionine enkephalin, respectively). Methionine enkephalin-induced dilation was attenuated by **Rp 8**-bromo **cAMPs** (10(-5) M), a cAMP antagonist (7 +/- 1, 11 +/- 1 and 17 +/- 1 vs. 2 +/- 1, 4 +/- 1, and 7 +/- 1% for methionine enkephalin 10(-10), 10(-8), and 10(-6) M in the absence and presence of **Rp 8**-bromo **cAMPs**, respectively). Dilation by the other endogenous and synthetic opioid analogues was also accompanied by elevated CSF cAMP and attenuated by **Rp 8**-bromo **cAMPs.**
Additionally, dilation produced by the cAMP analogue, 8-bromo cAMP, was blunted by iberiotoxin. These data show that both cAMP and activation of Kca+2 channels contribute to opioid-induced pial artery dilation. Further, these data suggest that opioids elicit dilation, at least in part, via the sequential release of cAMP and subsequent activation of Kca+2 channels by this second messenger.

L10 ANSWER 11 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97176758 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9024297
TITLE: Guanosine 3',5'-cyclic monophosphate-dependent protein kinase II mediates heat-stable enterotoxin-provoked chloride secretion in rat intestine.
AUTHOR: Vaandrager A B; Bot A G; De Jonge H R
CORPORATE SOURCE: Department of Biochemistry, Cardiovascular Research Institute COEUR, Medical Faculty, Erasmus University, Rotterdam, The Netherlands.
SOURCE: Gastroenterology, **(1997 Feb)** 112 (2) 437-43.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970321
Last Updated on STN: 19970321
Entered Medline: 19970313
AB BACKGROUND & AIMS: Escherichia coli heat-stable enterotoxins (STa) provoke electrogenic Cl- secretion in the intestine through a guanosine 3',5'-cyclic monophosphate (cGMP)-dependent signal transduction pathway. The cGMP receptor involved in the activation of the Cl- channel is not known with certainty but may comprise either adenosine 3',5'-cyclic monophosphate (cAMP)-dependent protein kinase (cAK) or cGMP-dependent protein kinase (cGK) type II. The aim of this study was to discriminate between these possibilities using specific kinase inhibitors. METHODS: Intestinal electrogenic Cl- secretion was determined by measuring short-circuit current (Isc) in a Ussing chamber. RESULTS: The general protein kinase inhibitors staurosporine and H-8 inhibited rat cGK II activity in vitro with 50% inhibitory concentration values of 4 nmol/L and 3 mumol/L, respectively, which are lower than those reported for cAK. Both staurosporine and H-8, when added to rat proximal colon at concentrations that did not affect the Isc response to 8-bromo-cAMPS, inhibited the STa- and 8-bromo-cGMP-provoked Isc response for more than 80%. Furthermore, the relative specific cGK inhibitor Rp isomer of 8-(chlorophenylthio)-cGMP, but not the cAK inhibitor RP isomer of (**Rp**) **8**-bromo-**cAMPS**, inhibited the Isc response to submaximal levels of STa in rat proximal colon. CONCLUSIONS: These data provide further evidence for an important role of cGK II in STa-mediated Cl- secretion in native rat intestinal epithelium.

L10 ANSWER 12 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97161053 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9008325
TITLE: A possible role for nitric oxide in the regulation of human

ureteral smooth muscle tone in vitro.
AUTHOR: Stief C G; Uckert S; Truss M C; Becker A J; Machtens S; Jonas U
CORPORATE SOURCE: Department of Urology, Hannover Medical School, Germany.
SOURCE: Urological research, **(1996)** 24 (6) 333-7.
Journal code: 0364311. ISSN: 0300-5623.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970422
Last Updated on STN: 19970422
Entered Medline: 19970408

AB There is ample evidence that nitric oxide (NO) is an important neurotransmitter in many tissues of the urogenital tract. The aim of the present study was to examine the possible role of NO in ureteral relaxation. Human ureteral rings were mounted in organ bath chambers and precontracted in KCl. Increasing doses of the NO donor linsidomine (SIN-1) were added with and without prior blockade of the NO/cGMP pathway by methylene blue and protein kinase (PK) inhibitors Rp-8-pCPT-cGMPS and **RP-8**-CPT-**cAMPS.** Electrical filed stimulation (EFS) was done before and after incubation with L-NOARG (NG-nitro-L-arginine) and TTX (tetratodoxin). For detection of neuronal NO synthase (NOS), ureters were stained immunohistochemically. Ureteral strips were dose dependently relaxed by SIN-1; preincubation with methylene blue and protein kinase G inhibitor significantly reduced the SIN-1-induced relaxations. No effects of L-NOARG and TTX on EFS-induced tone alterations were found. NOS-positive neuronal axons and nerve-ending-like structures were found in the muscular layers. Our in vitro findings suggest that ureteral relaxation may involve the NO pathway.

L10 ANSWER 13 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97133033 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8978392
TITLE: Role of nitric oxide, cyclic nucleotides, and the activation of ATP-sensitive K+ channels in the contribution of adenosine to hypoxia-induced pial artery dilation.
AUTHOR: Armstead W M
CORPORATE SOURCE: Department of Anesthesia, University of Pennsylvania, Philadelphia, USA.
SOURCE: Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism, **(1997 Jan)** 17 (1) 100-8.
Journal code: 8112566. ISSN: 0271-678X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970121

AB Previously, it had been observed that nitric oxide (NO) contributes to hypoxia-induced pial artery dilation in the newborn pig. Additionally, it was also noted that activation of ATP-sensitive K+ channels (KATP) contribute to cGMP-mediated as well as to hypoxia-induced pial dilation. Although somewhat controversial, adenosine is also thought to contribute to hypoxic cerebrovasodilation. The present study was designed to investigate the role of NO, cyclic nucleotides, and activation of KATP channels in the elicitation of adenosine's vascular response and relate these mechanisms to the contribution of adenosine to hypoxia-induced pial artery dilation. The closed cranial window technique was used to measure pial diameter in newborn pigs. Hypoxia-induced artery dilation was

attenuated during moderate (PaO2 approximately 35 mm Hg) and severe hypoxia (PaO2 approximately 25 mm Hg) by the adenosine receptor antagonist 8-phenyltheophylline (8-PT) (10(-5) M) (26 +/- 2 vs. 19 +/- 2 and 34 +/- 2 vs. 22 +/- 2% for moderate and severe hypoxia in the absence vs. presence of 8-PT, respectively). This concentration of 8-PT blocked pial dilation in response to adenosine (8 +/- 2, 16 +/- 2, and 23 +/- 2 vs. 2 +/- 2, 4 +/- 2, and 6 +/- 2% for 10(-8), 10(-6), and 10(-4) M adenosine before and after 8-PT, respectively). Similar data were also obtained using adenosine deaminase as a probe for the role of adenosine in hypoxic pial dilation. Adenosine-induced dilation was associated with increased CSF cGMP concentration (390 +/- 11 and 811 +/- 119 fmol/ml for control and 10(-4) M adenosine, respectively). The NO synthase inhibitor, L-NNA, and the cGMP antagonist, Rp 8-bromo cGMPs, blunted adenosine-induced pial dilation (8 +/- 1, 14 +/- 1, and 20 +/- 3 vs. 3 +/- 1, 5 +/- 1, and 8 +/- 3% for 10(-8), 10(-6), and 10(-4) M adenosine before and after L-NNA, respectively). Adenosine dilation was also blunted by glibenclamide, a KATP antagonist (9 +/- 2, 14 +/- 3, 21 +/- 4 vs. 4 +/- 1, 8 +/- 2, and 11 +/- 2% for 10(-8), 10(-6), and 10(-4) M adenosine before and after glibenclamide, respectively). Finally, it was also observed that adenosine-induced dilation was associated with increased CSF cAMP concentration and the cAMP antagonist, **Rp** 8-bromo **cAMPs**, blunted adenosine pial dilation. These data show that adenosine contributes to hypoxic pial dilation. These data also show that NO, cGMP, cAMP, and activation of KATP channels all contribute to adenosine induced pial dilation. Finally, these data suggest that adenosine contributes to hypoxia-induced pial artery dilation via cAMP and activation of KATP channels by NO and cGMP.

L10 ANSWER 14 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97083240 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8929814
TITLE: Anisoosmotic regulation of hepatic gene expression.
AUTHOR: Warskulat U; Newsome W; Noe B; Stoll B; Haussinger D
CORPORATE SOURCE: Medizinische Universitatsklinik, Klinik fur Gastroenterologie, Hepatologie und Infektiologie, Heinrich-Heine-Universitat, Dusseldorf, Germany.
SOURCE: Biological chemistry Hoppe-Seyler, **(1996 Jan)** 377 (1) 57-65.
Journal code: 8503054. ISSN: 0177-3593.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 19980206
Entered Medline: 19970320

AB The effect of anisoosmolarity on the abundance of various mRNA species was examined in perfused rat liver and H4IIE rat hepatoma cells. Hyperosmotic exposure (385 mosmol/l) of isolated rat livers increased mRNA levels for tyrosine aminotransferase (TAT) by 246% and those for phosphoenolpyruvate carboxykinase (PEPCK) by 186%, whereas hypoosmotic exposure (225 mosmol/l) decreased their levels to 43% and 42%, respectively. mRNA levels for fructose-1,6-bisphosphatase (FBP), argininosuccinate lyase (ASL), argininosuccinate synthetase (ASS), glutamine synthetase (GS), glutaminase (GA) and glucokinase (GK) were largely unaffected. In H4IIE cells the modulation of TAT and PEPCK mRNA levels by anisoosmotic exposure was similar to that found in perfused rat liver. ASL and glutaminase mRNA levels were influenced in an opposite manner. The effects of anisoosmolarity on PEPCK mRNA levels in H4IIE cells were largely abolished in the presence of the protein kinase inhibitors H-7, H-89 and HA-1004. Other protein kinase inhibitors such as Go-6850, KN-62, **Rp**-8-CPT-**cAMPS**, rapamycin, wortmannin, genistein or herbimycin did not prevent the osmosensitivity of PEPCK mRNA levels. Also pertussis and cholera toxin, vanadate and colchicine did not affect the

osmosensitivity of PEPCK mRNA levels. The data suggest that anisoosmotic exposure acts on the levels of some but not all mRNA species and that this action may involve changes in protein phosphorylation. They further indicate that the recently identified osmosensitive signal transduction pathway which involves a G-protein and tyrosine kinase dependent activation of mitogen-activated protein kinases is apparently not involved in the osmoregulation of PEPCK mRNA levels.

L10 ANSWER 15 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97061148 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8905178
TITLE: Effects of activation and inhibition of cAMP-dependent protein kinase on long-term habituation in the crab Chasmagnathus.
AUTHOR: Romano A; Locatelli F; Delorenzi A; Pedreira M E; Maldonado H
CORPORATE SOURCE: Facultad de Ciencias Exactas y Naturales, Departamento de Ciencias Biologicas, Pab 2. University of Buenos Aires, Argentina.. aromano@biolo.bg.uba.edu.ar
SOURCE: Brain research, **(1996 Sep 30)** 735 (1) 131-40.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970227
Last Updated on STN: 19970227
Entered Medline: 19970211

AB On sudden presentation of a danger stimulus, the crab Chasmagnathus elicits an escape response that habituates promptly and for a long period. We have previously reported that administration of a cAMP-permeable analog (CPT-cAMP) along with a phosphodiesterase inhibitor (IBMX) improves long-term habituation (LTH). In present experiments we studied the effect of systemic administration of the protein kinase A (PKA) activator Sp-5,6-DCl-cBIMPS and that of the PKA inhibitor **Rp-8**-Cl-**cAMPS** on LTH tested 24 h after a weak training protocol (5 trials of danger stimulus presentation) or a strong training protocol (15-30 trials), respectively. A 50 microliters pre-training injection of 75 microM Sp-5,6-DCl-cBIMPS, and to a lesser degree of 25 microM, improved retention of the habituated response but not affect short-term habituation (STH). Like pre-training injection, post-training administration of Sp-5,6-DCl-cBIMPS proved to exert a facilitatory action on retention though with 75 microM dose only. Conversely, both pre- and post-training injection of 25 microM **Rp-8**-Cl-**cAMPS** impaired LTH without affecting STH. Thus, the PKA activator Sp-5,6-DCl-cBIMPS enables a weak training to produce LTH while the PKA inhibitor **Rp-8**-Cl-**cAMPS** impairs LTH when a strong training is given. Activation of crab PKA by Sp-5,6-DCl-cBIMPS and its inhibition by **Rp-8**-Cl-**cAMPS** were assessed using an in vitro PKA activity assay. These results provide independent evidences supporting the view that PKA plays a key role in long-term memory storage in this learning paradigm.

L10 ANSWER 16 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97060598 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8904645
TITLE: Effect of cyclic GMP-dependent vasodilators on the expression of inducible nitric oxide synthase in vascular smooth muscle cells: role of cyclic AMP.
AUTHOR: Boese M; Busse R; Mulsch A; Schini-Kerth V
CORPORATE SOURCE: Zentrum der Physiologie, Klinikum der Johann Wolfgang Goethe Universitat, Frankfurt/Main, Germany.
SOURCE: British journal of pharmacology, **(1996 Oct)** 119 (4) 707-15.

Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970305
Last Updated on STN: 19970305
Entered Medline: 19970218

AB 1. In the present study we examined whether interleukin-1 beta (IL-1 beta) increases the activity of adenylyl cyclase in vascular smooth muscle cells and determined its role in the cytokine-induced expression of the inducible nitric oxide synthase (iNOS) and activation of nuclear transcription factor-kappa B (NF-kappa B). In addition the interaction between cyclic AMP- and cyclic GMP-elevating agonists on the IL-1 beta-stimulated expression of iNOS was examined. 2. Exposure of vascular smooth muscle cells to IL-1 beta stimulated the formation of cyclic AMP but not of cyclic GMP. The intracellular level of cyclic AMP reached a maximum within 1 h and then gradually declined over the next 5 h. This IL-1 beta (60 u ml-1)-stimulated formation of cyclic AMP was modest (about 3 fold at 60 u ml-1 for 1 h) compared to that evoked by isoprenaline (about 9 fold at 3 x 10(-6) M for 2 min). 3. The IL-1 beta (60 u ml-1 for 24 h)-stimulated accumulation of nitrite, which was taken as an index of NO production, was concentration-dependently increased by preferential inhibitors of cyclic AMP-dependent phosphodiesterases (rolipram and trequinsin). This effect was reproduced by a specific activator of the cyclic AMP-dependent protein kinase(s) A, Sp-8-CPT-cAMPS (10(-4) M) but was prevented by a specific inhibitor of cyclic AMP-dependent protein kinase(s) A, **Rp-8-CPT-cAMPS** (10(-4) M).
These compounds alone [rolipram (10(-6) M), trequinsin (3 x 10(-6) M) and Sp-8-CPT-cAMPS (10(-4) M)] slightly but significantly increased the release of nitric oxide while **Rp-8-CPT-cAMPS**
elicited no such effect. 4. Inducible NOS protein was expressed in IL-1 beta (30 u ml-1, 24 h)-stimulated smooth muscle cells as assessed by Western blot analysis. The level of iNOS protein was markedly increased in smooth muscle cells which had been exposed to IL-1 beta in combination with either rolipram (3 x 10(-6) M) or Sp-8-CPT-cAMPS (10(-4) M) but was reduced in those exposed to IL-1 beta and **Rp-8-CPT-cAMPS** (10(-4) M). A weak expression of iNOS protein was found in smooth muscle cells which had been exposed to either Sp-8-CPT-cAMPS or rolipram alone for 24 h while **Rp-8-CPT-cAMPS**
elicited no such effect. 5. Exposure of smooth muscle cells to IL-1 beta (30 u ml-1) for 30 min increased the level of NF-kappa B-DNA complexes in nuclear extracts as detected by electrophoretic mobility shift assay. Similar levels of NF-kappa B-DNA complexes were found in cells which had been exposed to IL-1 beta in combination with either Sp-8-CPT-cAMPS (10(-4) M), trequinsin (10(-6) M) or rolipram (10(-6) M). None of the modulators alone affected the basal level of NF-kappa B binding activity. 6. NO-donors [sodium nitroprusside (SNP) 10(-4) M; dinitrosyl-iron-di-L-cysteine-complex (DNIC), 10(-4) M; 3-morpholino-sydnonimine (SIN-1), 10(-4) M] and atrial natriuretic factor (10(-6) M) significantly increased the IL-1 beta (30 or 60 u ml-1, 24 h)-stimulated expression of iNOS protein and activity as assessed indirectly by the conversion of oxyhaemoglobin to methaemoglobin. In the absence of IL-1 beta, SNP (10(-4) M, 24 h) but not the other cyclic GMP-dependent vasodilators caused a modest expression of iNOS protein. No such effect was found in smooth muscle cells exposed to SNP in combination with **Rp-8-CPT-cAMPS** (10(-4) M) while an increased level of iNOS
protein was found in those exposed to SNP in combination with either Sp-8-CPT-cAMPS (10(-4) M) or rolipram (3 x 10(-6) M). 7. Exposure of vascular smooth muscle cells to either S-nitroso-L-cysteine (Cys-SNO, 10(-4) M), SNP (10(-4) M) or SIN-1 (10(-4) M) for 35 min affected minimally the basal activation of NF-kappa B but abolished that evoked by IL-1 beta (30 u ml-1 added during the last 30 min). However, addition of Cys-SNO following the stimulation with IL-1 beta (during the last 5 min of

the 30 min exposure period) reduced the level of NF-kappa B-DNA complexes only slightly. 8. These data indicate that the cyclic AMP-dependent pathway plays a decisi

L10 ANSWER 17 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97053577 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9019713
TITLE: Hypoxic inhibition of K+ currents in isolated rat type I carotid body cells: evidence against the involvement of cyclic nucleotides.
AUTHOR: Hatton C J; Peers C
CORPORATE SOURCE: Institute for Cardiovascular Research, Leeds University, Leeds LS2 9JT, UK.
SOURCE: Pflugers Archiv : European journal of physiology, **(1996 Nov-Dec)** 433 (1-2) 129-35.
Journal code: 0154720. ISSN: 0031-6768.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970227
Last Updated on STN: 20021210
Entered Medline: 19970211

AB Whole-cell patch-clamp recordings were used to evaluate the effects of the cyclic nucleotides adenosine 3',5'-cyclic monophosphate (cAMP) and guanosine 3',5'-cyclic monophosphate (cGMP) on ionic currents in type I carotid body cells isolated from rat pups, and to investigate whether cyclic nucleotides are involved in K+ current inhibition by hypoxia. In the presence of 500 microM isobutylmethylxanthine, currents were not significantly modified by 8-bromo-cAMP (2 mM), dibutyryl-cAMP (5 mM) or 8-bromo-cGMP (2 mM). Currents were also unaffected by the phosphodiesterase (PDE)-resistant protein kinase A activators Sp-cyclic adenosine-3', 5'-monophosphorothioate (Sp-cAMPS) and Sp-8-bromoadenosine-3', 5'-monophosphorothioate (Sp-8-bromo-cAMPS) (50 microM), or by beta-phenyl-1,N2-ethenoguanosine-3',5'-cyclic monophosphate (PET-cGMP) (100 microM) or the nitric oxide donor S-nitroso-N-acetylpenicillamine (SNAP; 500 microM). Ca2+ channel currents were also unaffected by Sp-8-Br-cAMPS, PET-cGMP and SNAP at the same concentrations. In the absence of cyclic nucleotide analogues, hypoxia (PO2 17-23 mmHg) reversibly inhibited K+ currents. This degree of hypoxic inhibition was not significantly altered by the PDE-resistant protein kinase A inhibitors Rp-cyclic adenosine-3', 5'-monophosphorothioate (Rp-**cAMPS**) (50 microM) or **Rp**-8-bromoadenosine-3',5'-monophosphorothioate (**Rp**-8-bromo-**cAMPS**) (200 microM). Similarly, PET-cGMP (100 microM) and SNAP (500 microM) did not alter the degree of inhibition caused by hypoxia. At the same concentrations used in type I cell experiments, Sp-8-bromo-cAMPS, PET-cGMP and SNAP completely relaxed isolated guinea-pig basilar arteries preconstricted with 20 mM K+-containing solutions. Our results indicate that cyclic nucleotides alone are not an important factor in the regulation by O2 tension of K+ currents in rat type I carotid body cells.

L10 ANSWER 18 OF 25 MEDLINE on STN
ACCESSION NUMBER: 96438725 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8841085
TITLE: Rp diastereomeric analogs of cAMP inhibit both cAMP- and cGMP-induced dilation of hamster mesenteric small arteries.
AUTHOR: Jackson W F
CORPORATE SOURCE: Department of Biological Sciences, College of Arts and Sciences, Western Michigan University, Kalamazoo 49008, USA.
CONTRACT NUMBER: HL 32469 (NHLBI)
SOURCE: Pharmacology, **(1996 Apr)** 52 (4) 226-34.
Journal code: 0152016. ISSN: 0031-7012.

PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970110

AB Cross talk between the adenosine (3',5'-cyclic monophosphate) (cAMP) and the guanosine (3',5'-cyclic monophosphate) (cGMP) signalling pathways in vascular smooth muscle may occur such that cAMP may act through cGMP-dependent protein kinase rather than cAMP-dependent protein kinase to induce relaxation of this tissue. Therefore, it was hypothesized that due to this crosstalk, competitive antagonists of cAMP may not show much selectivity in inhibition of cAMP- or cGMP-induced vasodilation. To test this hypothesis, the effects of Rp-diastereomeric phosphorothioate derivatives of cAMP, putative competitive antagonists of cAMP at cAMP-dependent protein kinase, were assessed on vasodilation induced by Sp-phosphorothioate derivatives of cAMP, dibutyryl cAMP, 8-Br cGMP and sodium nitroprusside. Hamster mesenteric arteries (200-400 microns i.d.) were cannulated and pressurized to 75 mm Hg and constricted to approximately 50% of maximum with 1 mumol/l phenylephrine. Vasodilators were then added in cumulative fashion and diameter responses recorded in the absence and presence of (Rp)-adenosine (3',5'-cyclic monophosphorothioate) (Rp **cAMPs**) or (**Rp**)-**8**-(parachlorophenylthio) adenosine (3',5'-cyclic monophosphorothioate) (Rp 8CPT cAMPs). Rp cAMPs (0.1-0.5 mmol/l) inhibited dilations induced by the cAMP agonists, (Sp)-adenosine (3',5'-cyclic monophosphorothioate) (Sp cAMPs) and dibutyryl cAMP, but also inhibited dilations induced by 8-Br cGMP and sodium nitroprusside ($p < 0.05$ and $n > 4$ for all). In a more detailed study we found that Rp 8CPT cAMPs against Sp 8CPT cAMPs (3.6 +/- 1.2) was similar to the pA2 for Rp 8CPT cAMPs against 8-Br cGMP (4.1 +/- 1.2) ($p > 0.05$, d.f. = 37). These data support the hypothesis that both cAMP and cGMP act through a common protein kinase to cause vasodilation and urge caution in the use of Rp-diastereomeric analogs of cyclic nucleotides to dissect out specific signal transduction pathways in blood vessels.

L10 ANSWER 19 OF 25 MEDLINE on STN
ACCESSION NUMBER: 96196759 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8607997
TITLE: Cyclic AMP mediates a presynaptic form of LTP at cerebellar parallel fiber synapses.
AUTHOR: Salin P A; Malenka R C; Nicoll R A
CORPORATE SOURCE: Department of Cellular and Molecular Pharmacology, University of California, San Francisco 94143-0450, USA.
SOURCE: Neuron, **(1996 Apr)** 16 (4) 797-803.
Journal code: 8809320. ISSN: 0896-6273.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199605
ENTRY DATE: Entered STN: 19960605
Last Updated on STN: 19980206
Entered Medline: 19960528

AB The N-methyl-D-aspartate receptor-independent form of long-term potentiation (LTP) at hippocampal mossy fiber synapses requires presynaptic Ca(2+)-dependent activation of adenylyl cyclase. To determine whether this form of LTP might occur at other synapses, we examined cerebellar parallel fibers that, like hippocampal mossy fiber synapses, express high levels of the Ca2+/calmodulin-sensitive adenylyl cyclase I. Repetitive stimulation of parallel fibers caused a long-lasting increase in synaptic strength that was associated with a decrease in paired-pulse facilitation. Blockade of glutamate receptors did not prevent LTP

induction, nor did loading of Purkinje cells with a Ca2+ chelator. LTP was occluded by forskolin-induced potentiation and blocked by the protein kinase A inhibitor **Rp-8-CPT-cAMPS.** These findings suggest that parallel fiber synapses express a form of LTP that is dependent on the activation of a presynaptic adenylyl cyclase and is indistinguishable from LTP at hippocampal mossy fiber synapses.

L10 ANSWER 20 OF 25 MEDLINE on STN
ACCESSION NUMBER: 96012478 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7572340
TITLE: Hormonal control of hepatic glutaminase.
AUTHOR: Brosnan J T; Ewart H S; Squires S A
CORPORATE SOURCE: Department of Biochemistry, Memorial University of Newfoundland, St. John's, Canada.
SOURCE: Advances in enzyme regulation, **(1995)** 35 131-46.
Journal code: 0044263. ISSN: 0065-2571.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19980206
Entered Medline: 19951026

AB (1) Glucagon activates hepatic glutaminase in vivo. Mitochondria from glucagon-injected rats retain an enhanced capacity to catabolize glutamine and this is more sensitive to activation by inorganic phosphate. The glucagon-elicited stimulation of glutaminase is not evident in broken mitochondria. A similar activation of glutaminase occurs in a number of situations which are associated with elevated glucagon levels in vivo, i.e., after a high-protein meal, after injection of bacterial endotoxin and in diabetes mellitus. (2) Studies in isolated hepatocytes revealed that glutaminase could be activated, not only by glucagon, but also by a cell-permeable protein kinase A activator (Sp-cAMPS) and by a cell-permeable protein phosphatase 1 and 2A inhibitor (okadaic acid). However, the activation of glutaminase by glucagon was not inhibited by a cell-permeable protein kinase A inhibitor (**Rp-8-Br-cAMPS**). We suggest that the signalling pathway, for glutaminase activation by glucagon, is complex and possibly contains redundant elements.

L10 ANSWER 21 OF 25 MEDLINE on STN
ACCESSION NUMBER: 95386509 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7657638
TITLE: Novel (Rp)-cAMPS analogs as tools for inhibition of cAMP-kinase in cell culture. Basal cAMP-kinase activity modulates interleukin-1 beta action.
AUTHOR: Gjertsen B T; Mellgren G; Otten A; Maronde E; Genieser H G; Jastorff B; Vintermyr O K; McKnight G S; Doskeland S O
CORPORATE SOURCE: Department of Anatomy and Cell Biology, University of Bergen, Norway.
CONTRACT NUMBER: GM 32875 (NIGMS)
ML 44948
SOURCE: Journal of biological chemistry, **(1995 Sep 1)** 270 (35) 20599-607.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951013
Last Updated on STN: 19970203
Entered Medline: 19951004

AB Novel (Rp)-cAMPS analogs differed widely in ability to antagonize cAMP

activation of pure cAMP-dependent protein kinase I and II and to antagonize actions of cAMP on gene expression, shape change, apoptosis, DNA replication, and protein phosphorylation in intact cells. These differences were related to different abilities of the analogs to stabilize the holoenzyme form relative to the dissociated form of cAMP kinase type I and II. (**Rp**)-**8**-Br-**cAMPS** and (**Rp**)-**8**-Cl-**cAMPS** were the most potent cAMP antagonists for isolated type I kinase and for cells expressing mostly type I kinase, like IPC-81 leukemia cells, fibroblasts transfected with type I regulatory subunit (RI), and primary hepatocytes. It is proposed that (**Rp**)-**8**-Br-**cAMPS** or (**Rp**)-**8**-Cl-**cAMPS** should replace (Rp)-**cAMPS** as the first line cAMP antagonist, particularly for studies in cells expressing predominantly type I kinase. The phosphorylation of endogenous hepatocyte proteins was affected oppositely by (**Rp**)-**8**-Br-**cAMPS** and increased cAMP, indicating that (**Rp**)-**8**-Br-**cAMPS** inhibited basal cAMP-kinase activity. The inhibition of basal kinase activity was accompanied by enhanced DNA replication, an effect which could be reproduced by microinjected mutant cAMP-subresponsive RI. It is concluded that the basal cAMP-kinase activity exerts a tonic inhibition of hepatocyte replication. (**Rp**)-**8**-Br-**cAMPS** and microinjected RI also desensitized hepatocytes toward inhibition of DNA synthesis by interleukin-1 beta. This indicates that basal cAMP-kinase activity can have a permissive role for the action of another (interleukin-1 beta) signaling pathway.

L10 ANSWER 22 OF 25 MEDLINE on STN
ACCESSION NUMBER: 95301553 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7782324
TITLE: Regulation of RCK1 currents with a cAMP analog via enhanced protein synthesis and direct channel phosphorylation.
AUTHOR: Levin G; Keren T; Peretz T; Chikvashvili D; Thornhill W B; Lotan I
CORPORATE SOURCE: Department of Physiology and Pharmacology, Sackler School of Medicine, Tel-Aviv University, Ramat Aviv, Israel.
CONTRACT NUMBER: NS-29633 (NINDS)
SOURCE: Journal of biological chemistry, **(1995 Jun 16)** 270 (24) 14611-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199507
ENTRY DATE: Entered STN: 19950726
Last Updated on STN: 19950726
Entered Medline: 19950717

AB We have recently shown that the rat brain Kv1.1 (RCK1) voltage-gated K+ channel is partially phosphorylated in its basal state in Xenopus oocytes and can be further phosphorylated upon treatment for a short time with a cAMP analog (Ivanina, T., Perts, T., Thornhill, W. B., Levin, G., Dascal, N., and Lotan, I. (1994) Biochemistry 33, 8786-8792). In this study, we show, by two-electrode voltage clamp analysis, that whereas treatments for a short time with various cAMP analogs do not affect the channel function, prolonged treatment with 8-bromoadenosine 3',5'-cyclic monophosphorothioate ((Sp)-8-Br-cAMPS), a membrane-permeant cAMP analog, enhances the current amplitude. It also enhances the current amplitude through a mutant channel that cannot be phosphorylated by protein kinase A activation. The enhancement is inhibited in the presence of (**Rp**)-**8**-Br-**cAMPS**, a membrane-permeant protein kinase A inhibitor. Concomitant SDS-polyacrylamide gel electrophoresis analysis reveals that this treatment not only brings about phosphorylation of the wild-type channel, but also increases the amounts of both wild-type and mutant channel proteins; the latter effect can be inhibited by cycloheximide, a protein synthesis inhibitor. In the presence of

cycloheximide, the (Sp)-8-Br-cAMPS treatment enhances only the wild-type current amplitudes and induces accumulation of wild-type channels in the plasma membrane of the oocyte. In summary, prolonged treatment with (Sp)-8-Br-cAMPS regulates RCK1 function via two pathways, a pathway leading to enhanced channel synthesis and a pathway involving channel phosphorylation that directs channels to the plasma membrane.

L10 ANSWER 23 OF 25 MEDLINE on STN
ACCESSION NUMBER: 95165158 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7861174
TITLE: Effects of arachidonic acid on dopamine synthesis, spontaneous release, and uptake in striatal synaptosomes from the rat.
AUTHOR: L'hirondel M; Ĉheramy A; Godeheu G; Glowinski J
CORPORATE SOURCE: INSERM U114, College de France, Paris.
SOURCE: Journal of neurochemistry, **(1995 Mar)** 64 (3) 1406-9.
Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950404
Last Updated on STN: 19950404
Entered Medline: 19950317

AB Arachidonic acid (AA) markedly stimulated, in a dose-dependent manner, the spontaneous release of [3H]dopamine ([3H]DA) continuously synthesized from [3H]tyrosine in purified synaptosomes from the rat striatum. As estimated by simultaneous measurement of the rate of [3H]H2O formation (an index of [3H]tyrosine conversion into [3H]DOPA), the AA response was associated with a progressive and dose-dependent reduction of [3H]DA synthesis. In contrast to AA, arachidonic acid, oleic acid, and the methyl ester of AA (all at 10(-4) M) did not modify [3H]DA release. The AA (3 x 10(-5) M)-evoked release of [3H]DA was not affected by inhibiting AA metabolism, with either 5,8,11,14-eicosatetraynoic acid or metyrapone, suggesting that AA acts directly and not through one of its metabolites. AA also inhibited in a dose-dependent manner [3H]DA uptake into synaptosomes, with a complete blockade observed at 10(-4) M. However, AA (10(-4) M) still stimulated [3H]DA spontaneous release in the presence of either nomifensine or other DA uptake inhibitors, indicating that AA both inhibits DA reuptake and facilitates its release process. Finally, the AA (10(-4) M)-evoked release of [3H]DA was not affected by protein kinase A inhibitors (H-89 or **Rp-8-Br-cAMPS**) but was markedly reduced in the presence of protein kinase C inhibitors (Ro 31-7549 or chelerythrine).

L10 ANSWER 24 OF 25 MEDLINE on STN
ACCESSION NUMBER: 94235325 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8179921
TITLE: Theophylline suppresses human alveolar macrophage respiratory burst through phosphodiesterase inhibition.
AUTHOR: Dent G; Giembycz M A; Rabe K F; Wolf B; Barnes P J; Magnussen H
CORPORATE SOURCE: Krankenhaus Grosshansdorf, LVA Hamburg, Germany.
SOURCE: American journal of respiratory cell and molecular biology, **(1994 May)** 10 (5) 565-72.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940621
Last Updated on STN: 19940621

Entered Medline: 19940614

AB The effects of theophylline upon human alveolar macrophage function were assessed and compared with its action upon macrophage cyclic nucleotide phosphodiesterase (PDE) activity and cyclic adenosine monophosphate (cAMP) levels. In the concentration range of 10 mumol/liter to 1 mmol/liter, theophylline caused a concentration-dependent inhibition of opsonized zymosan-stimulated hydrogen peroxide (H2O2) generation and PDE-catalyzed cAMP hydrolysis and increased the cellular cAMP content. Macrophage H2O2 generation was also inhibited by forskolin, an activator of adenylyl cyclase, but whereas theophylline (1 mmol/liter) and forskolin (1 mumol/liter) exhibited a synergic elevation of macrophage cAMP, there was no synergy between the two agents in the inhibition of respiratory burst. The inhibition of H2O2 generation by theophylline was reversed by the competitive inhibitor of cAMP-dependent protein kinase, (Rp)8-bromoadenosine cyclic 3':5'-monophosphorothioate (**Rp-8-Br-cAMPS**; 100 mumol/liter), indicating that the functional effect of theophylline was mediated through the elevation of cAMP. The inhibition of H2O2 generation by theophylline was not affected by adenosine deaminase (0.1 U/ml), indicating that the inhibition did not involve adenosine antagonism. It is concluded that theophylline exerts a direct inhibitory action upon human alveolar macrophage function through the elevation of cAMP levels as a result of PDE inhibition, and that this effect is observed at concentrations of theophylline that may be achieved in serum during therapy.

L10 ANSWER 25 OF 25 MEDLINE on STN
ACCESSION NUMBER: 92233411 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1314695
TITLE: Unhydrolyzable analogues of adenosine 3':5'-monophosphate demonstrating growth inhibition and differentiation in human cancer cells.
AUTHOR: Yokozaki H; Tortora G; Pepe S; Maronde E; Genieser H G; Jastorff B; Cho-Chung Y S
CORPORATE SOURCE: Cellular Biochemistry Section, National Cancer Institute, Bethesda, Maryland 20892.
SOURCE: Cancer research, **(1992 May 1)** 52 (9) 2504-8. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920612
Last Updated on STN: 19970203
Entered Medline: 19920526

AB A set of adenosine 3':5'-monophosphate (cAMP) analogues that combine exocyclic sulfur substitutions in the equatorial (Rp) or the axial (Sp) position of the cyclophosphate ring with modifications in the adenine base of cAMP were tested for their effect on the growth of HL-60 human promyelocytic leukemia cells and LS-174T human colon carcinoma cells. Both diasteromeres of the phosphorothioate derivatives were growth inhibitory, exhibiting a concentration inhibiting 50% of cell proliferation of 3-100 microM. Among the analogues tested, **Rp-8-Cl-cAMPS** and Sp-8-Br-cAMPS were the two most potent. **Rp-8-Cl-cAMPS** was 5- to 10-fold less potent than 8-Cl-cAMP while Sp-8-Br-cAMPS was approximately 6-fold more potent than 8-Br-cAMP. The growth inhibition was not due to a block in a specific phase of the cell cycle or due to cytotoxicity. **Rp-8-Cl-cAMPS** enhanced its growth-inhibitory effect when added together with 8-Cl-cAMP and increased differentiation in combination with N6-benzyl-cAMP. The binding kinetics data showed that these Sp and Rp modifications brought about a greater decrease in affinity for Site B than for Site A of RI (the regulatory subunit of type I cAMP-dependent protein kinase) and a substantial decrease of affinity for Site A of RII (the regulatory subunit of type II protein kinase) but only a small

decrease in affinity for Site B of RII, indicating the importance of the Site B binding of RII in the growth-inhibitory effect. These results show that the phosphorothioate analogues of cAMP are useful tools to investigate the mechanism of action of cAMP in growth control and differentiation and may have practical implication in the suppression of malignancy.

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NEWS	2		"Ask CAS" for self-help around the clock
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NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB

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